Minutes of Meeting

Alabama Medicaid Agency
Pharmacy and Therapeutics Committee

February 10, 2010

Members Present: Chair, Dr. Lucy Culpepper, Ms. Janet Allen, Dr. Gerard Ferris, Dr. Kelli Littlejohn, Mr. Ben Main, Dr. Robert Moon, Ms. LaTonage Porter, Dr. Nancy Sawyer, Dr. Joseph Thomas and Dr. Chivers Woodruff

Members Absent: Dr. Michelle Freeman

Presenters: Dr. Tina Hisel

Presenters Present via teleconference: Dr. Laureen Biczak

1. OPENING REMARKS

Dr. Culpepper called the Pharmacy and Therapeutics (P&T) Committee Meeting to order at 9:10 a.m.

2. APPROVAL OF MINUTES

Dr. Culpepper asked if there were any corrections to the minutes from the November 18, 2009 P&T Committee Meeting.

There were no objections. Dr. Ferris made a motion to approve the minutes as presented and Dr. Woodruff seconded to approve the minutes. The minutes were unanimously approved.

3. PHARMACY PROGRAM UPDATE

Dr. Littlejohn noted that a routine Preferred Drug List (PDL) update was completed in January 2010. The Agency has developed a NDC-specific report to assist providers with determining the PDL status of covered prenatal vitamins. The report is available on the Agency's website (www.medicaid.alabama.gov).

An ALERT was sent to providers in January 2010 to address physician-administered drugs. In 2008, the Agency began requiring NDCs for the top 20 physician-administered multiple source drugs. The Agency is now expanding this requirement to all drugs. Effective March 1, 2010, providers will receive an informational denial code, but the claim will not be denied. Effective July 1, 2010, the NDC will be mandatory on all physician-administered drugs billed either electronically or on paper CMS-1500 or UB-04 claim forms.

Effective February 1, 2010, the Agency began covering smoking cessation products for pregnant females as a component of the Maternity Care Program. Recipients must be enrolled and receiving counseling services through the Alabama Department of Public Health's Quitline. Prior Authorizations for these drugs will be administered through the Pharmacy Administrative Contractor, Health Information Designs, Inc.

Effective March 1, 2010, new cost savings measures will be implemented related to the fiscal agent, HP (formerly EDS). Changes are administrative in nature and pertain to the submission of paper claims, paper remittance advices (RAs) and paper reports. Claims/reports will primarily be handled electronically.

4. ORAL PRESENTATIONS BY MANUFACTURERS/MANUFACTURERS' REPRESENTATIVES

Five-minute verbal presentations were made on behalf of pharmaceutical manufacturers. The process and timing system for the manufacturers' oral presentations was explained. The drugs and corresponding manufacturers are listed below with the appropriate therapeutic class. There were a total of four manufacturer verbal presentations at the meeting.

5. PHARMACOTHERAPY CLASS REVIEWS (Please refer to the website for full text reviews.)

The pharmacotherapy class reviews began at approximately 9:15 a.m. There were a total of six re-reviews and one new drug review. The behavioral health classes were last reviewed in November 2007.

Alzheimer's Agents: Parasympathomimetic (Cholinergic) Agents, American Hospital Formulary Service (AHFS) 120400 and Central Nervous System Agents, Miscellaneous, AHFS 289200

Manufacturer comments on behalf of these products:
Aricept® - Pfizer

Dr. Hisel commented that the agents that are included in this review are listed in Table 1. This class includes four cholinesterase inhibitors and the NMDA receptor antagonist, memantine. All of the agents are available in an oral formulation; rivastigmine is also available in a transdermal patch formulation. During the previous review of this class, there were no generic products available; however, galantamine has since become available in both an immediate- and extended-release generic formulation. In addition, the FDA recently approved the first generic version of donepezil orally disintegrating tablets in December 2009.

Current treatment guidelines that incorporate the use of the Alzheimer's agents are summarized in Table 2, several of which have been updated since this class was last reviewed. According to these guidelines, the primary goal of treatment is to delay the progression of symptoms and preserve

functional ability. The use of a cholinesterase inhibitor may lead to modest improvements in some patients; therefore, it is appropriate to offer a trial of one of these agents for patients with mild-to-moderate disease. Memantine can be considered for the treatment of patients with moderate-to-severe disease either as monotherapy or in combination with a cholinesterase inhibitor. Donepezil, galantamine and rivastigmine are preferred over tacrine due to hepatotoxicity and dosing frequency. Otherwise, the available guidelines do not give preference to one agent over another. Clinicians should base treatment decisions on tolerability, adverse events and ease of use.

The FDA-approved indications are noted in Table 3. The cholinesterase inhibitors are all approved for the treatment of mild-to-moderate disease. Donepezil is also approved for the treatment of severe disease. Memantine has only been approved by the FDA for the treatment of moderate-to-severe Alzheimer's disease. Although these agents provide symptomatic benefit, they have not been shown to delay the progression of neurodegeneration.

The Alzheimer's agents are generally well tolerated; however, gastrointestinal adverse events occur more frequently with the cholinesterase inhibitors than with memantine. Dizziness is the most common adverse event with memantine. The use of tacrine is commonly associated with elevations in serum aminotransferase levels.

Numerous clinical trials have evaluated the efficacy and safety of the cholinesterase inhibitors and memantine, which are summarized in Table 8. Several different outcomes have been assessed using more than 40 different instruments, including cognition, global function, behavior and quality of life. There is consistent evidence from well-designed trials that donepezil, galantamine, rivastigmine and memantine positively affect cognition and global function, although the improvements are modest. The findings are less consistent for other outcomes, including behavior and quality of life. In most cases, the duration of well-designed clinical trials were less than one year. There are very few studies that directly compare the various agents. Most of the trials have compared active treatment to placebo or no treatment. The published studies also differ with regards to design, patient population and treatment duration, which make it difficult to directly compare the results.

Dr. Hisel concluded that there is insufficient evidence to support that one brand Alzheimer's agent is more efficacious than another. Formulations without a generic alternative should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand products within the class reviewed, with the exception of tacrine, are comparable to each other and to the generics and offer no significant clinical advantage over other alternatives in general use. Tacrine possesses an extensive adverse event profile compared to the other brands and generics, and should be managed through the existing medical justification portion of the prior authorization process.

No brand Alzheimer's agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

No brand tacrine product is recommended for preferred status, regardless of cost.

Dr. Ferris asked about the effect of these drugs on outcomes such as time to institutionalization. Dr. Hisel responded that the data are inconsistent and stated that it is likely very patient-specific.

Dr. Ferris commented that there is little information about determining if an Alzheimer's agent is working for a particular patient and when to discontinue therapy. Dr. Hisel stated that individual goals of therapy need to be established for each patient. If the goals are no longer being met, then the provider/family needs to decide on whether treatment should be continued or discontinued.

There was no further discussion on the agents in this class. Dr. Culpepper asked the P&T Committee Members to mark their ballots.

Antidepressants: AHFS 281604

Manufacturer comments on behalf of these products:

Pristiq® - Pfizer

Dr. Hisel commented that the agents that are included in this review are listed in Table 1. All of the antidepressants are available in an oral formulation, except the selegiline patch. The antidepressants are categorized into 6 different subclasses, including monoamine oxidase inhibitors (MAOIs), selective serotonin- and norepinephrine-reuptake inhibitors (SNRIs), selective serotonin-reuptake inhibitors (SSRIs), serotonin modulators, tricyclic antidepressants (TCAs) and miscellaneous agents. The majority of the products are available in a generic formulation, and there is at least one generic product available in each antidepressant subclass.

Desvenlafaxine (Pristiq®) and milnacipran (Savella®) are new SNRIs that have been approved by the FDA since this class was last reviewed. Desvenlafaxine is an extended-release tablet approved for the treatment of major depressive disorder. It is the major active metabolite of venlafaxine. Milnacipran is only approved for the treatment of fibromyalgia. Dr. Hisel informed the Committee that since the time the clinical review packet was prepared and printed, milnacipran was reassigned to a new AHFS Class 284000 (fibromyalgia agents). Therefore, this agent will not be included in this review. The fibromyalgia class is new and has not been previously reviewed by the P&T Committee. She noted that there are no other products, other than milnacipran, in the fibromyalgia class.

For the treatment of major depressive disorder, many studies have demonstrated similar efficacy among the antidepressants, either with agents in the same subclass or among agents in different subclasses. The available guidelines do not give preference to one particular agent over another. The selection of an antidepressant should be based on tolerability, adverse events, and patient preference.

For panic disorder, either an SNRI or SSRI is recommended as initial therapy due to their favorable safety and tolerability profiles. SSRIs are also recommended for the long-term treatment of generalized anxiety disorder and obsessive-compulsive disorder. The SNRIs, SSRIs and TCAs have all been shown to be more effective than placebo for the treatment of anxiety disorders, and comparative studies have demonstrated similar efficacy among the antidepressants. Guidelines do

not give preference to one particular agent over another. The choice of treatment should be based on safety, adverse events, drug interactions, prior response to treatment and comorbid conditions.

For the treatment of premenstrual dysphoric disorder, SSRIs are recommended as initial therapy given either intermittently or continuously. Studies have demonstrated efficacy in reducing both physical and behavioral symptoms.

Since this class was last reviewed, duloxetine has also been approved by the FDA for the treatment of fibromyalgia. It has been shown to relieve pain to a greater extent than placebo in clinical trials. The American Pain Society recommends the use of TCAs or SSRIs as one of several initial treatment options for patients with fibromyalgia. It should be noted that these guidelines were published in 2005 and they do not provide recommendations regarding the use of the SNRIs for the treatment of fibromyalgia.

Although the MAOIs are an effective treatment option for patients with major depressive disorder, drug interactions, dietary restrictions and serious adverse events limit their use. Guidelines recommend that the MAOIs be reserved for patients who are not responding to other treatment options. Selegiline is available in a transdermal formulation and the clinical data for the 6 mg/24 hour strength indicate that a modified diet is not required at this dose. However, data are limited for the 9 mg/24 hour and 12 mg/24 hour strengths. Patients receiving these doses should follow the dietary modifications required for patients taking MAOIs.

All of the antidepressants carry a boxed warning regarding the increased risk of suicidal thinking and behavior in children, adolescents and young adults compared with placebo in short-term studies of major depressive disorder and other psychiatric disorders. In addition, cases of life-threatening hepatic failure have been reported in patients treated with nefazodone.

Dr. Hisel concluded that there is insufficient evidence to support that one brand antidepressant is more efficacious than another within its given indication. Formulations without a generic alternative should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand products within the class reviewed, with the exception of the monoamine oxidase inhibitors, are comparable to each other and to the generics and offer no significant clinical advantage over other alternatives in general use. The monoamine oxidase inhibitors possess an extensive adverse effect profile compared to the other brands and generics and should be managed through the existing medical justification portion of the prior authorization process.

No brand antidepressant is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

No brand monoamine oxidase inhibitor is recommended for preferred status, regardless of cost.

There was no further discussion on the agents in this class. Dr. Culpepper asked the P&T Committee Members to mark their ballots.

Cerebral Stimulants/Agents Used for ADHD: Amphetamines, AHFS 282004, Anorexigenic Agents and Respiratory and Cerebral Stimulants, Miscellaneous, AHFS 282092, and Central Nervous System Agents, Miscellaneous, AHFS 289200

Manufacturer comments on behalf of these products:

Vyvanse® - Shire

Focalin XR® - Novartis

Dr. Hisel commented that the agents that are included in this review are listed in Table 1. They include amphetamines, methylphenidate derivatives and atomoxetine, which are all approved for the treatment of ADHD. In addition, armodafinil and modafinil are cerebral stimulants approved for the treatment of sleep disorders. Armodafinil is a new stimulant that has been approved by the FDA since this class was last reviewed. It is the R-enantiomer of modafinil, which is a mixture of the R- and S-enantiomers. The cerebral stimulants are available in a variety of dosage forms, which primarily differ in their release mechanism and duration of action. Table 2 classifies the agents based on their duration of action. All of the agents are available in an oral formulation and methylphenidate is also available in a transdermal formulation. Several of the products are available generically, including the long-acting form of mixed amphetamine salts.

The amphetamines and methylphenidate derivatives are classified as Schedule II controlled substances. Armodafinil and modafinil are classified as Schedule IV controlled substances. Atomoxetine is not considered a cerebral stimulant; therefore, it is not classified as a controlled substance.

For the initial treatment of ADHD, the American Academy of Child and Adolescent Psychiatry recommends the use of an agent approved by the FDA and they do not give preference to one agent over another. Other organizations recommend the initial use of a cerebral stimulant for the treatment of ADHD; atomoxetine is recommended for patients with comorbid anxiety disorders, tics, sleep disorders, substance abuse, stimulant failure, or adverse events with stimulants. The stimulants and atomoxetine have been shown to be effective for the treatment of ADHD in a variety of clinical trials. Although comparative trials have been conducted, it is challenging to directly compare the results of these studies due to differences in design, variable outcomes, small sample sizes, and short duration of follow-up. There are several factors to take into consideration when selecting a pharmacologic agent for the treatment of children and adolescents with ADHD. This includes the presence of comorbid conditions, patient/family preference, storage and administration at school, history of substance abuse, drug diversion, pharmacokinetics and adverse events.

The American Academy of Sleep Medicine guidelines for the treatment of narcolepsy state that amphetamines, methylphenidate and modafinil are all effective for the treatment of daytime sleepiness due to narcolepsy. Modafinil is also recommended as one of several initial treatment options for individuals with excessive sleepiness due to obstructive sleep apnea and shift work sleep disorder. Armodafinil was approved by the FDA in June 2007 and is not addressed in the available guidelines. Although both modafinil and armodafinil have been shown to be more effective than placebo, there were no studies found in the medical literature directly comparing these agents to each other, or to other cerebral stimulants.

There is a boxed warning describing the risk of dependence and abuse for the amphetamines and methylphenidate derivatives. There is also a boxed warning regarding the increased risk of suicidal ideation in short-term studies in children or adolescents with ADHD who were treated with atomoxetine.

Dr. Hisel concluded that there is insufficient evidence to support that one brand cerebral stimulant or agent used for ADHD is more efficacious than another within its given indication. There is at least one short-acting, intermediate-acting and long-acting agent available in a generic formulation. Formulations without a generic alternative should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand products within the class reviewed are comparable to each other and to the generics and offer no significant clinical advantage over other alternatives in general use.

No brand cerebral stimulant/agent used for ADHD is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Dr. Woodruff asked why there is not a recommendation to use a non-controlled substance, like atomoxetine, over the cerebral stimulants which are more likely to be diverted or abused. Dr. Hisel replied that while atomoxetine should be considered when there is a concern regarding diversion or abuse, the cerebral stimulants can be used safely if appropriately monitored. Dr. Littlejohn noted that the prior authorization criteria allow for the use of atomoxetine if there is a concern regarding abuse.

Mr. Main asked about the effects of these agents on long-term growth, specifically when there are drug holidays incorporated during the summer months. Dr. Hisel replied that she was not familiar with the specific results of studies that evaluated the effects on height when drug holidays are used. Dr. Culpepper commented that in her patient population, there may be slight variations in the growth curves; however, most are maintained on the growth curve. She further stated that is why they follow their patients closely to monitor for changes in growth and development. Dr. Littlejohn also noted that there are allowances for drug holidays in the prior authorization criteria.

Dr. Thomas asked if there was any information on the percentage of children who continue to take stimulants as adults. Dr. Hisel replied that she was not familiar with that particular data. Dr. Woodruff asked Dr. Thomas what percent of patients are diagnosed with ADHD for the first time as adults. Dr. Thomas commented approximately 3-5% of his patients fit this profile. Dr. Hisel stated that, based on some available information, approximately 30% to 70% of children with ADHD manifest symptoms into adulthood. She also noted that 1% to 7% of adults experience ADHD symptoms; however, these statistics do not provide information on the percentage of children or adults that are currently receiving treatment for ADHD.

There was no further discussion on the agents in this class. Dr. Culpepper asked the P&T Committee Members to mark their ballots.

Anxiolytics, Sedatives, and Hypnotics – Barbiturates: AHFS 282404
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that mephobarbital and phenobarbital are available in a generic formulation. The barbiturates are approved for the treatment of insomnia and for the induction of sedation. Some agents are also approved for use as an adjunct to anesthesia, as well as for the treatment of seizure disorders.

Currently, there are no clinical guidelines that recommend the use of a barbiturate as first-line therapy for any condition in an outpatient setting. There are few clinical trials available that directly compare the various agents. Some studies suggest that the barbiturates are not as effective as other sedative-hypnotic agents.

The use of barbiturates is associated with abuse, psychological and physical dependence. Tolerance to the sedative-hypnotic effects occurs rapidly, and these agents lose their effectiveness for sleep induction and maintenance after 2 weeks.

Dr. Hisel concluded that there is insufficient evidence to support that one brand barbiturate agent is safer or more efficacious than another. Therefore, all brand agents within the class reviewed are comparable to each other and to the generics and offer no significant clinical advantage over other alternatives in general use.

No brand barbiturate is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Dr. Woodruff asked if the barbiturates were being evaluated as sedative/hypnotic agents only, not for use as antiepileptics. Dr. Hisel replied that this review focused on the sedative/hypnotic indications for these agents. She commented that antiepileptic drugs fall outside of the scope of the PDL.

There was no further discussion on the agents in this class. Dr. Culpepper asked the P&T Committee Members to mark their ballots.

Anxiolytics, Sedatives, and Hypnotics – Benzodiazepines: AHFS 282408
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the agents that are included in this review are listed in Table 1. Benzodiazepines are an optional drug class in accordance with the Omnibus Budget Reconciliation Act of 1990 (OBRA 90). There are several brand and generic products that are not currently covered by Alabama Medicaid. However, this review included all dosage forms and strengths, regardless of coverage status. All of the benzodiazepines are available in a generic formulation, with the exception of quazepam.

These agents are used primarily for the treatment of anxiety disorders and for the short-term treatment of insomnia. In addition, some of the agents are approved for the treatment of seizure disorders, acute alcohol withdrawal, as well as for the induction and maintenance of general anesthesia. The benzodiazepines are mechanistically similar; however, they differ with regards to their pharmacokinetic properties.

The American Psychiatric Association recommends the initial use of either a SNRI or SSRI for the treatment of panic disorder. However, benzodiazepines may be preferred for patients with very distressing or impairing symptoms in whom rapid symptom control is critical. They can be used concurrently with antidepressants to help control symptoms until the antidepressant takes effect, which is then followed by a slow tapering of the benzodiazepine. For the long-term treatment of generalized anxiety disorder, SSRIs are recommended as first-line therapy. Benzodiazepines may be used for acute treatment, but they should generally not used beyond 2 to 4 weeks. Benzodiazepines have been shown to be more effective than placebo, and have demonstrated similar efficacy compared to agents in other classes for the treatment of anxiety disorders. Guidelines do not give preference to one particular benzodiazepine over another. The risk of adverse events and physiological dependence must be considered when using the benzodiazepines. These agents are not recommended as monotherapy for the treatment of obsessive-compulsive disorder or posttraumatic stress disorder.

The American Academy of Sleep Medicine recommends the use of a short or intermediate-acting benzodiazepine, a benzodiazepine receptor agonist, or ramelteon for the initial treatment of insomnia. They do not give preference to one agent over another. Results from clinical trials demonstrate that the benzodiazepines are effective for the short-term treatment of insomnia. Symptom pattern, treatment goals, past treatment responses, patient preference, comorbid conditions, contraindications, drug interactions and adverse events should be considered when selecting a specific agent. The frequency and severity of adverse events may be lower with benzodiazepine receptor agonists due to their shorter half-lives.

Benzodiazepines may also be used for the treatment of seizure disorders, either as monotherapy or adjunctive therapy. It was noted that other antiepileptic drugs are not currently included in the PDL. Diazepam is available in a rectal gel formulation, which is specifically indicated for the management of selected, refractory, patients with epilepsy who require intermittent use of diazepam to control bouts of increased seizure activity. This product provides a beneficial route of administration compared to other agents in this class.

Dr. Hisel concluded that there is insufficient evidence to support that one benzodiazepine (brand or generic) is more efficacious than another. Therefore, all benzodiazepines within the class reviewed, with the exception of diazepam rectal gel, are comparable to each other and offer no significant clinical advantage over other alternatives in general use. Diazepam rectal gel offers significant clinical advantages in general use over the other brands and generics in the class.

No brand benzodiazepine, with the exception of diazepam rectal gel, is recommended for preferred status. Alabama Medicaid should consider not covering brand benzodiazepines.

Alabama Medicaid should consider covering all generic benzodiazepines.

Diazepam rectal gel (Diastat® and Diastat AcuDial®) is recommended for preferred status.

Dr. Thomas asked about why there was so little difference in cost between brand and generic clonazepam. Dr. Hisel replied that she did not have specific information regarding the pricing schedule for these products.

Dr. Ferris asked if there was any evidence that any one agent maintained normal sleep architecture better than others. Dr. Hisel replied that there was not a lot of new literature that has been published with the benzodiazepines for the treatment of insomnia. She noted that the benzodiazepines differ with regards to onset, duration of action, and metabolites; therefore, the agents may affect sleep architecture differently. Dr. Biczak added that there have been no consistent findings in well controlled trials that conclusively indicate that any change or lack of change in sleep architecture clearly improved outcomes or effectiveness.

Dr. Ferris commented that these agents are only approved for the short-term treatment of insomnia and it is challenging to get patients to adhere to sleep hygiene regimens. Dr. Hisel agreed that the benzodiazepines should only be used for the short-term treatment of insomnia. She stated that the next class review includes miscellaneous sedatives, in which some agents have been studied for up to 6 months. She commented that the use of a pharmacologic agent for the chronic treatment of insomnia is still somewhat controversial, unless there are underlying comorbid conditions. Dr. Ferris stated that other pharmacologic agents with hypnotic side effects (such as antidepressants) are often used in patients with comorbid conditions, like fibromyalgia. Dr. Thomas commented that the most common underlying disease which produces disturbances in sleep is depression; therefore, the use of an antidepressant would be appropriate.

Dr. Woodruff commented about the use of topical forms of benzodiazepines in hospice patients. He asked if these products were being compounded or if they were available in a commercial formulation. Dr. Hisel replied that she was not aware of any topical benzodiazepine that was available commercially. Dr. Woodruff asked if the topical compounded benzodiazepines were covered by Medicaid. Dr. Littlejohn stated that compounded claims are reimbursed depending on drug coverage status of the ingredients She reminded the Committee that the barbiturates and benzodiazepines are an optional drug coverage class for Medicaid. Since these agents are covered for non-dual eligible recipients, CMS mandates that these drug classes are also covered for dual eligible recipients. Dr. Thomas commented that retrograde amnesia is common with the benzodiazepines and that he uses clonazepam to taper his patients off these agents, particularly short-acting agents.

There was no further discussion on the agents in this class. Dr. Culpepper asked the P&T Committee Members to mark their ballots.

Anxiolytics, Sedatives, and Hypnotics – Miscellaneous: AHFS 282492
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the agents that are included in this review are listed in Table 1. Buspirone, chloral hydrate, droperidol, hydroxyzine, meprobamate, zaleplon and zolpidem are available in a generic formulation. These agents are primarily used for the treatment of anxiety disorders and insomnia.

Eszopiclone, zaleplon and zolpidem are classified as benzodiazepine receptor agonists. Compared to the benzodiazepines, they have a more rapid onset, shorter duration of action, and a lower risk of tolerance, dependence and abuse. They are classified as Schedule IV controlled substances by federal regulation. Ramelteon is a melatonin receptor agonist. Discontinuation after chronic administration did not produce withdrawal signs and it does not appear to produce physical dependence; therefore, it is not a controlled substance.

The agents that are approved for the treatment of anxiety disorders include buspirone, hydroxyzine and meprobamate. The American Psychiatric Association recommends the initial use of either a SNRI or a SSRI for the treatment of panic disorder due to their favorable safety and tolerability profiles. Buspirone and sedating antihistamines are not effective as for the treatment of panic disorder. For the long-term treatment of generalized anxiety disorder, the use of an SSRI is recommended as first-line therapy. Sedating antihistamines are one of several options for the short-term, intermediate treatment of generalized anxiety disorder. Buspirone is not recommended for the initial treatment of obsessive-compulsive disorder or posttraumatic stress disorder. The available guidelines do not provide any recommendations regarding the use of meprobamate for the treatment of anxiety disorders.

Chloral hydrate, eszopiclone, ramelteon, zaleplon and zolpidem are approved for the treatment of insomnia. The American Academy of Sleep Medicine recommends the use of a short or intermediate-acting benzodiazepine, benzodiazepine receptor agonist, or ramelteon for the initial treatment of insomnia. They do not give preference to one agent over another. Chloral hydrate is not recommended for the treatment of insomnia. Symptom pattern, treatment goals, past treatment responses, patient preference, comorbid conditions, contraindications, drug interactions and adverse events should be considered when selecting a specific agent. The frequency and severity of adverse events may be lower with the benzodiazepine receptor agonists and ramelteon than benzodiazepines. Results from clinical trials demonstrate that these agents are effective for the treatment of insomnia. The clinical trials performed in support of efficacy for eszopiclone, ramelteon and zolpidem ER were up to 6 months in duration. There were very few studies found in the medical literature which directly compared the efficacy and safety of these agents.

Droperidol is effective for the prevention/treatment of nausea and vomiting from surgical and diagnostic procedures. However, cases of QT prolongation and/or torsade de pointes have been reported in patients receiving droperidol. Some cases have occurred in patients with no known risk factors for QT prolongation, and some cases have been fatal. Due to its potential for serious proarrhythmic effects and death, droperidol should be reserved for patients who fail to respond to other adequate treatments.

Dr. Hisel concluded that there is insufficient evidence to support that one brand miscellaneous anxiolytic, sedative or hypnotic agent is more efficacious than another within its given indication. Formulations without a generic alternative should be managed through the medical justification

portion of the prior authorization process.

Therefore, all brand products within the class reviewed are comparable to each other and to the generics and offer no significant clinical advantage over other alternatives in general use.

No brand miscellaneous anxiolytic, sedative or hypnotic is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Dr. Thomas asked if propofol was included in this review. Dr. Hisel replied that this product was not included in this AHFS class.

There was no further discussion on the agents in this class. Dr. Culpepper asked the P&T Committee Members to mark their ballots.

6. **NEW DRUG REVIEW**
Samsca® (tolvaptan) AHFS Class 402892 – Diuretics, Miscellaneous
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that tolvaptan is an oral vasopressin V_2 receptor antagonist, which was approved by the FDA in May 2009. It is indicated for the treatment of clinically significant euvolemic and hypervolemic hyponatremia (serum sodium <125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including patients with heart failure, cirrhosis, and Syndrome of Inappropriate Antidiuretic Hormone (SIADH). There are no generic tolvaptan products available.

The use of a traditional diuretic leads to water and electrolyte excretion. Whereas, the use of tolvaptan leads to an increase in water excretion only, a decrease in urine osmolality, and an increase in serum sodium concentration. Urinary excretion of sodium and potassium, as well as plasma potassium concentrations, are not significantly affected by tolvaptan.

The management of hyponatremia depends on the clinical presentation and duration of the disease. Treatment options include fluid restriction, sodium chloride administration and diuresis. Patients with chronic mild hyponatremia are often asymptomatic and treatment consists of just fluid restriction or isotonic saline administration. However, acute severe hyponatremia requires more aggressive initial therapy as it may increase morbidity and mortality. Treatment of hyponatremia must be approached carefully as overly rapid correction may cause osmotic demyelination. Symptoms of osmotic demyelination are often irreversible and include quadriparesis, paraparesis, dysphagia, dysarthria, diplopia, seizures, coma and death.

There are limited guidelines available that discuss the management of hyponatremia. An expert panel provided treatment recommendations in 2007, which includes fluid restriction, sodium chloride administration and diuresis. The panel concluded that the optimal use of the vasopressin receptor antagonists has not been determined and further studies are needed.

Three short-term studies were conducted in a small number of patients with euvolemic or hypervolemic hyponatremia. The results demonstrated significant improvements in serum sodium concentrations compared to fluid restriction or placebo. Several other studies have evaluated the use of tolvaptan in patients with heart failure as add-on therapy to conventional treatments. Significant changes in body weight have been observed; however, the long-term use of tolvaptan (median duration 9.9 months) failed to demonstrate any improvements in mortality or hospitalizations for worsening heart failure.

Data supporting the use of tolvaptan are limited. It has not been established that raising serum sodium with tolvaptan provides a symptomatic benefit to patients. Patients requiring intervention to raise serum sodium urgently should not be treated with tolvaptan. Hospitalization is required for initiation and reinitiation of tolvaptan therapy so that serum sodium can be monitored closely.

Dr. Hisel concluded that there is insufficient evidence to conclude that tolvaptan offers a significant clinical advantage over other alternatives in general use. Since tolvaptan is not indicated as first-line therapy for the management of hyponatremia, it should be managed through the medical justification portion of the prior authorization process.

No brand tolvaptan product is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Dr. Ferris commented that hyponatremia may be a significant problem in psychiatric patients. He asked what would be necessary for providers to prescribe this medication if prior authorization was required. Dr. Hisel replied that the prior authorization criteria are still being developed and would follow the FDA-approved indications (as listed above). Dr. Littlejohn noted that tolvaptan needs to be initiated in the hospital setting. Dr. Ferris asked that if this drug was started in an inpatient setting, could it be continued in the outpatient setting. Dr. Littlejohn stated that this drug could be continued in the outpatient setting. She reiterated that the criteria are still being developed and they would be consistent with the FDA-approved indications.

Dr. Woodruff asked about the coverage status of tolvaptan. Dr. Littlejohn stated that this drug is covered and prior authorization is currently required. It was noted that there have been no prior authorization requests for this product to date.

Dr. Ferris asked if there are any alternative drugs that are mechanistically similar to tolvaptan. Dr. Hisel replied that there is an injectable vasopressin receptor antagonist currently available as well. Dr. Culpepper asked why the tablets were the only product to be reviewed today. Dr. Hisel replied that this new drug pharmacotherapy review focused solely on tolvaptan. She stated that there is not a class review that includes the other miscellaneous diuretics. Dr. Woodruff asked that, in the inpatient setting, would the parental form be covered. Dr. Littlejohn stated that in the inpatient setting, there is no prior authorization required. Dr. Moon reiterated that there are no limitations in the inpatient setting.

Dr. Thomas asked an additional question pertaining to the Cerebral Stimulants/Agents Used for ADHD class review. The question was in regards to why Cephalon would create Nuvigil® after marketing Provigil®, and asked if it was due to patent expiration issues. Dr. Hisel replied that she was not familiar with the reason this product was developed by Cephalon. Dr. Biczak stated that variations of molecules are often created due to the potential for decreased side effects, increased efficacy, or patent extension.

There was no further discussion on the agents in this class. Dr. Culpepper asked the P&T Committee Members to mark their ballots.

7. RESULTS OF VOTING ANNOUNCED

The results of voting for each of the therapeutic classes were announced; all classes were approved as recommended. Results of voting are described in the Appendix to the minutes.

8. NEW BUSINESS

There was no new business.

9. NEXT MEETING DATE

The next P&T Committee Meeting is scheduled for May 12, 2010 at the Medicaid Building. Additional meetings will be held on August 11, 2010 and November 10, 2010.

10. ADJOURN

There being no further business, Mr. Main moved to adjourn and Dr. Woodruff seconded.

The meeting was adjourned at 10:30 a.m.

Appendix

RESULTS OF THE BALLOTING
Alabama Medicaid Agency
Pharmacy and Therapeutics Committee
February 10, 2010

A. Recommendation: No brand Alzheimer's agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands. No brand tacrine product is recommended for preferred status, regardless of cost.

Amendment: None

Vote: Approve as recommended (5 of 6 votes)

Medical Director	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Deputy Commissioner	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Commissioner	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action

B. Recommendation: No brand antidepressant is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands. No brand monoamine oxidase inhibitor is recommended for preferred status, regardless of cost.

Amendment: None

Vote: Unanimous to approve as recommended

Medical Director	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Deputy Commissioner	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Commissioner	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action

C. **Recommendation:** No brand cerebral stimulant/agent used for ADHD is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Medical Director	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Deputy Commissioner	☑ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Commissioner	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action

D. **Recommendation:** No brand barbiturate is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Medical Director	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Deputy Commissioner	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Commissioner	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action

E. Recommendation: No brand benzodiazepine, with the exception of diazepam rectal gel, is recommended for preferred status. Alabama Medicaid should consider not covering brand benzodiazepines. Alabama Medicaid should consider covering all generic benzodiazepines. Diazepam rectal gel (Diastat® and Diastat AcuDial®) is recommended for preferred status.

Amendment: None

Vote: Unanimous to approve as recommended

Medical Director	☒	Approve	☐	Approve as amended	☐	Disapprove	☐ No action
Deputy Commissioner	☒	Approve	☐	Approve as amended	☐	Disapprove	☐ No action
Commissioner	☒	Approve	☐	Approve as amended	☐	Disapprove	☐ No action

F. Recommendation: No brand miscellaneous anxiolytic, sedative, or hypnotic is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Medical Director	☒	Approve	☐	Approve as amended	☐	Disapprove	☐ No action
Deputy Commissioner	☒	Approve	☐	Approve as amended	☐	Disapprove	☐ No action
Commissioner	☒	Approve	☐	Approve as amended	☐	Disapprove	☐ No action

G. **Recommendation:** No brand tolvaptan product is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Medical Director	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Deputy Commissioner	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Commissioner	☒ Approve	☐ Approve as amended	☐ Disapprove	☐ No action

Respectfully submitted,

Tina Hisel, Pharm.D., BCPS

February 10, 2010
Date